Claims

1. The use of an angiotensin derivative comprising at least one angiotensin peptide moiety coupled to a peptide carrier-binding moiety in the manufacture of a medicament for use in combatting diseases associated with the renin-angiotensin system.

2. The use as claimed in claim 1 wherein the angiotensin moiety comprises angiotensin I or angiotensin II or a functional equivalent of angiotensin I or angiotensin II.

3. The use as claimed in claim 1 or claim 2 wherein the carrier binding moiety contains an amino acid residue having a reactive side chain.

4. The use as claimed in any one of the preceding claims wherein the carrier binding moiety is a peptide extension at the N- or the C-terminus of an angiotensin peptide moiety.

5. The use as claimed in any one of the preceding claims wherein the angiotensin derivative is of Formula I

$$((A)\text{-}X_n)_m\text{-}L_p\text{-}Y\text{-}[L_q(X_r\text{-}(A))_s]_t \qquad (I)$$

wherein

A represents an angiotensin peptide moiety;

X represents an amino acid;

Y represents an amino acid having a side chain with a free -SH, -OH or -COOH group;

L represents an organic linker capable of binding a group $((A)\text{-}X_n)$- at one or more sites, e.g. capable of binding up to 10 $(A)X_n$ moieties;

n and r are each = 0-20;

m and s are each ≥1, e.g. 1 to 10, preferably 1, 2, 3 or 4; and

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p, q and t are each 0 or 1;

wherein X may be attached at the N- or C-terminus of the angiotensin peptide moiety with the proviso that if $m \geq 2$, then p=1, or if $s \geq 2$, then q=1.

6. The use as claimed in claim 5 wherein A is an angiotensin peptide.

7. The use as claimed in any one of claims 5 or 6 wherein L is a peptide chain.

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8. The use as claimed in any one of claims 5 to 7 wherein n and r are each 0-10.

9. The use as claimed in any one of claims 5 to 8 wherein m and s are each ≤8.

10. The use as claimed in any one of claims 5 to 9 wherein X is an amino acid having no side chain or a hydrocarbyl side chain (preferably an alkyl, C_{3-7} cycloalkyl or cycloalkenyl, C_{3-7} cycloalkyl- or cycloalkenyl-alkyl, alkaryl, aralkyl or alkarylalkyl moiety in which each alkyl moiety may be saturated or unsaturated and contains up to 6 carbons and each aryl moiety is preferably a phenyl ring), particularly preferably an aliphatic side chain.

11. The use as claimed in any one of claims 5 to 10 wherein X is glycine, alanine, β-alanine, valine, leucine or isoleucine.

12. The use as claimed in any one of claims 5 to 11 wherein the angiotensin derivative is selected from

$$(A)\text{-}X_n\text{-}Y \qquad (II)$$

$$(A)\text{-}X_n\text{-}L\text{-}Y \qquad (III)$$

$((A)-X_n)_m-L-Y$ (IV)

$(A)-X_n-L-Y-L-X_r-(A)$ (V)

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wherein A, X, L, n and r are as hereinbefore defined and $m \geq 2$.

13. The use as claimed in any one of the preceding claims wherein the angiotensin derivative is selected from

(A)-Gly Cys

(A)-Cys

(A)-Tyr

N-acetyl-Cys-(A)

Tyr-(A)

N-acetyl-Cys-Gly-(A)

Cys - (A)

(A) - N-acetyl-Cys

where A is angiotensin I or II.

14. The use as claimed in any one of the preceding claims wherein the angiotensin derivative elicits a cross-reactive immune response with angiotensin I, angiotensin II, and/or angiotensinogen molecules.

15. The use as claimed in any one of the preceding claims wherein the angiotensin derivative is conjugated to a carrier.

16. The use as claimed in claim 15 wherein said carrier is a polypeptide.

17. The use as claimed in claim 16 wherein the carrier is selected from the purified protein derivative of tuberculin, tetanus toxoid, diphtheria toxoid, keyhole limpet haemocyanin or derivatives thereof.

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18. The use as claimed in any one of the preceding claims wherein said disease is congestive heart failure or hypertension.

19. The use as claimed in claim 18 for the modulation of blood pressure.

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20. A pharmaceutical composition comprising an angiotensin derivative as defined in any one of claims 1-14, or a conjugated angiotensin derivative as defined in any of claims 15 to 17, together with one or more pharmaceutically acceptable carriers or excipients.

21. An angiotensin derivative as defined in any one of claims 1-17 for use in therapy.

22. An angiotensin derivative of Formula I

$$((A)\text{-}X_n)_m\text{-}L_p\text{-}Y\text{-}[L_q(X_r\text{-}(A))_s]_t \qquad (I)$$

wherein

A represents an angiotensin I peptide moiety;

X represents an amino acid;

Y represents an amino acid having a side chain with a free -SH, -OH or -COOH group;

L represents an organic linker capable of binding a group $((A)\text{-}X_n)\text{-}$ at one or more sites, e.g. capable of binding up to 10 $(A)X_n$ moieties;

n and r are each = 0-20;

m and s are each ≥1, e.g. 1 to 10, preferably 1, 2, 3 or 4; and

p, q and t are each 0 or 1;

wherein X is attached at the N-terminus of the angiotensin peptide moiety with the proviso that if m≥2, then p=1, or if s≥2, then q=1.

23. An angiotensin derivative as claimed in any one of claim 22 wherein L is a peptide chain.

24. An angiotensin derivative as claimed in any one of claims 22 or 23 wherein n and r are each 0-10.

25. An angiotensin derivative as claimed in any one of claims 22 to 24 wherein m and s are each ≤8.

26. An angiotensin derivative as claimed in any one of claims 22 to 25 wherein X is an amino acid having no side chain or a hydrocarbyl side chain (preferably an alkyl, C_{3-7} cycloalkyl or cycloalkenyl, C_{3-7} cycloalkyl- or cycloalkenyl-alkyl, alkaryl, aralkyl or alkarylalkyl moiety in which each alkyl moiety may be saturated or unsaturated and contains up to 6 carbons and each aryl moiety is preferably a phenyl ring), particularly preferably an aliphatic side chain.

27. An angiotensin as claimed in any one of claims 22 to 26 wherein X is glycine, alanine, β-alanine, valine, leucine or isoleucine.

28. An angiotensin derivative as claimed in any one of claims 22 to 27 selected from

$$(A)\text{-}X_n\text{-}Y \qquad (II)$$

$$(A)\text{-}X_n\text{-}L\text{-}Y \qquad (III)$$

$$((A)\text{-}X_n)_m\text{-}L\text{-}Y \qquad (IV)$$

$$(A)-X_n-L-Y-L-X_r-(A) \qquad (V)$$

wherein A, X, L, n and r are as hereinbefore defined and $m \geq 2$.

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29. An angiotensin derivative as claimed in any one of claims 22 to 28 selected from

N-acetyl-Cys-(A)

Tyr-(A)

N-acetyl-Cys-Gly-(A)

Cys - (A)

where A is angiotensin I

30. An angiotensin derivative as claimed in any one of claims 22 to 29 which elicits a cross-reactive immune response with angiotensin I, angiotensin II, and/or angiotensinogen molecules.

31. An angiotensin derivative as claimed in any one of claims 22 to 30 conjugated to a carrier.

32. An angiotensin derivative as claimed in claim 31 wherein said carrier is a polypeptide.

33. An angiotensin derivative as claimed in claim 32 wherein the carrier is selected from the purified protein derivative of tuberculin, tetanus toxoid, diphtheria toxoid, keyhole limpet haemocyanin or derivatives thereof.

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34. A method of combatting conditions associated with activation of the renin-angiotensin system comprising

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administering an angiotensin derivative as defined in any one of claims 1-17.

35. A nucleic acid molecule coding for a linear angiotensin peptide derivative as claimed in any one of claims 1-17, and nucleic acid molecules with sequences complementary thereto.

36. An expression vector comprising a nucleic acid molecule as claimed in claim 35.

37. A host organism transformed with the vector of claim 36.

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38. A method of combatting conditions associated with the renin-angiotensin system comprising administering a nucleic acid molecule coding for a linear angiotensin peptide derivative as claimed in any one of claims 1-16 or an expression vector comprising a nucleic acid molecule coding for an angiotensin peptide derivative.

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39. A polypeptide immunogen capable when conjugated to a carrier of inducing antibodies in an immunised subject that recognise epitopes of angiotensin I, angiotensin II and/or angiotensinogen.

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